

Claims

1. Use of a virus, preferably an adenovirus, for the manufacture of a medicament, characterised in that the virus is replication deficient in cells which lack YB-1 in the nucleus, and whereby the virus encodes an oncogene or oncogene product, in particular an oncogene protein, which transactivates at least one viral gene, preferably an adenoviral gene, whereby the gene is selected from the group comprising E1B55kDa, E4orf6, E4orf3 and E3ADP.
2. Use of a virus, preferably an adenovirus, for the replication in cells which exhibit YB-1 in the nucleus, characterised in that the virus is replication deficient in cells which lack YB-1 in the nucleus, and whereby the virus encodes an oncogene or an oncogene product, in particular an oncogene protein, which transactivates at least one viral gene, preferably an adenoviral gene, whereby the gene is selected from the group comprising E1B55kDa, E4orf6, E4orf3 and E3ADP.
3. Use according to any of claims 1 or 2, characterised in that the virus, preferably the adenovirus, replicates in cells which have YB-1 in the nucleus.
4. Use according to any of claims 1 to 3, characterised in that the viral oncogene protein is E1A and/or the oncogene is the gene coding for E1A and/or the oncogene protein is E1A.
5. Use according to claim 4, characterised in that the viral oncogene protein E1A is capable of binding a functional Rb tumor suppressor gene product.
6. Use according to claim 4, characterised in that the viral oncogene protein E1A is incapable of binding a functional Rb tumor suppressor gene product.
7. Use according to any of claims 4 to 6, characterised in that the viral oncoprotein E1A does not induce nucleus localisation of YB-1.

8. Use according to any of claims 1 or 3 to 7, characterised in that the medicament is for patients whose cells are Rb positive or Rb negative.
9. Use according to claim 8, characterised in that the cells are those cells which are involved in the formation of the condition which is to be influenced by the medicament.
10. Use according to any of claims 1 to 9, characterised in that the cells are Rb negative and the cell nucleus is YB-1 positive, preferably YB-1 positive in the nucleus independent from the cell cycle.
11. Use according to any of claims 1 or 3 to 10, characterised in that the medicament is for the treatment of tumors.
12. Use according to claim 11, characterised in that the cells, preferably the cells forming the tumor or parts thereof, are resistant, preferably multiple resistant against pharmacological agents, preferably anti-tumor agents and more preferably cytostatics.
13. Use according to claim 12, characterised in that the cells express, preferably over-express of the membrane-anchored transport protein P glycoprotein.
14. Use according to any of claims 1 to 13, characterised in that the cells are p53 positive or p53 negative.
15. Use according to any of claims 5 or 7 to 14, characterised in that the oncogene protein exhibits one or several mutations or deletions compared to the wildtype oncogene protein E1A, whereby the deletion is preferably one selected from the group comprising deletions of the CR3 region and deletions of the N-terminus and deletions of the C-terminus.
16. Use according to claim 15, characterised in that the E1A oncogene protein is capable of binding to Rb.

17. Use according to any of claims 6 to 14, characterised in that the oncogene protein comprises one or several mutations or deletions compared to the wildtype oncogene protein, whereby the deletion is preferably a deletion in the CR1 region and/or CR2 region.
18. Use according to claim 17, characterised in that the oncogene protein E1A is incapable of binding to Rb.
19. Use according to any of claims 1 to 18, characterised in that the viral oncogene protein, preferably E1A, is under the control of a tissue and/or tumor specific promoter.
20. Use according to any of claims 1 to 19, characterised in that the virus, particularly the adenovirus, codes for YB-1.
21. Use according to claim 20, characterised in that YB- 1 is under the control of a tissue specific and/or tumor specific promoter.
22. Use according to any of claims 1 to 21, characterised in that the virus, preferably the adenovirus, codes for at least one protein, whereby the protein is selected from the group comprising E4orf6, E4orf3, E1B55k and adenoviral E3ADP protein.
23. Use according to any of claims 1 to 22, characterised in that the cells have YB-1 in the nucleus, preferably that the cells forming the tumor or part thereof have YB-1 in the nucleus.
24. Use according to any of claims 1 to 23, characterised in that the tumor comprises YB-1 in the nucleus after induction of the transport of YB-1 into the nucleus.

25. Use according to claim 24, characterised in that the transport of YB-1 is triggered by at least one measure selected from the group comprising irradiation, administration of cytostatics and hyperthermia.
26. Use according to claim 25, characterised in that the measure is applied to a cell, an organ or an organism.
27. Use according to any of claims 1 to 26, characterised in that the virus, preferably the adenovirus, is selected from the group comprising AdΔ24, dl922-947, E1Ad/01/07, dl1119/1131, CB 016, dl520 and viruses lacking an expressed viral oncogene which is capable of binding a functional Rb tumor suppressor gene product.
28. Use of a virus, preferably an adenovirus, for the manufacture of a medicament, whereby the virus, preferably the adenovirus, is designed such that the replication is controlled by YB-1 through the activation of the E2-late promoter, preferably the activation is predominantly controlled through the activation of the E2-late promoter.
29. Use of a virus, preferably an adenovirus, for replication in cells which have YB-1 in the nucleus, characterised in that the virus, preferably the adenovirus, is designed such that the replication is controlled by YB-1 through the activation of the E2-late promoter, preferably predominantly through the activation of the E2-late promoter.
30. Viral oncogene protein, preferably an isolated viral oncogene protein, characterised in that it comprises the following characteristics:
- a) transactivation of at least one viral gene, whereby the viral gene is selected from the group comprising E1B-55k, E3ADP and E4orf6 and E4orf3; and
 - b) lack of induction of YB-1 in a nucleus, preferably in the nucleus of the cell, in which the viral oncogene protein is present.

31. Viral oncogene protein according to claim 30, characterised in that the viral oncogene protein is E1A.

32. Viral oncogene protein according to claim 30 or 31, characterised in that the viral oncogene protein comprises one or several mutations or deletions compared to the wildtype oncogene protein, whereby the deletion is preferably selected from the group comprising deletion of the CR3 region, deletion of the N-terminus and deletion of the C-terminus.

33. Viral oncogene protein according to claim 32, characterised in that it is capable of binding to Rb.

34. Viral oncogene protein according to claim 30 or 31, characterised in that the viral oncogene protein comprises one or several mutations or deletions, whereby the deletion is preferably a deletion in the CR1 region and/or the CR2 region of the E1A oncogene protein.

35. Viral oncogene protein according to claim 34, characterised in that the viral oncogene protein is incapable of binding to Rb.

36. Use of a viral replication system, preferably an adenoviral replication system, comprising a nucleic acid coding for a virus, preferably an adenovirus, according to any of claims 1 to 29, and comprising a nucleic acid of a helper virus, whereby the nucleic acid of the helper virus comprises a nucleic acid sequence coding for YB-1.

37. Use of a viral replication system, preferably an adenoviral replication system according to claim 36, characterised in that the viral nucleic acid, preferably the adenoviral nucleic acid and/or the nucleic acid of the helper virus are present as replicable vectors.

38. Use of a nucleic acid coding for a virus, preferably an adenovirus according to any of claims 1 to 29, for the manufacture of a medicament, preferably for the manufacture of a medicament for the treatment of tumors.

39. Use according to claim 38, characterised in that the cells, preferably the cells forming the tumor or parts thereof, have a resistance, preferably a multiple resistance against

pharmacologically active agents, preferably anti-tumor agents and more preferably cytostatics.

40. Use of a nucleic acid coding for a virus, preferably an adenovirus according to any of claims 1 to 29, for replication in cells which have YB-1 in the nucleus, characterised in that the virus is replication deficient in cells which do not have YB-1 in the nucleus, and the virus encodes an oncogene or oncogene product which transactivates at least one viral gene, preferably an adenoviral gene, whereby the gene is selected from the group comprising E1B55kDa, E4orf6, E4orf3 and E3ADP.

41. Use of a nucleic acid coding for a virus, preferably an adenovirus, according to any of claims 1 to 29, for the manufacture of a medicament, whereby the virus is designed such that the replication is controlled by YB-1 through the activation of the E2-late promoter, preferably predominantly through the activation of the E2-late promoter.

42. Use of a nucleic acid coding for a virus, preferably an adenovirus, according to any of claims 1 to 29, for replication in cells, whereby the virus is designed such that the replication is controlled by YB-1 through the activation of the E2-late promoter, preferably predominantly through the activation of the E2-late promoter.

43. Use of a vector comprising a nucleic acid according to any of claims 36 to 42 for the use according to any of claims 1 to 29.

44. Use of a compound interacting with YB-1 for the characterisation of cells, cells of a tumor tissue or patients, in order to determine whether these shall be contacted with and/or treated by a virus, preferably an adenovirus, according to any of claims 1 to 29.

45. Use according to claim 44, characterised in that the means is selected from the group comprising antibodies, anticalines, aptamers, aptazymes and spiegelmers.

46. Use of the viral oncogene protein according to any of claims 30 to 35 or a nucleic acid coding therefor, for the manufacture of a virus, preferably an adenovirus, which may be used in connection with the uses as specified in any of claims 1 to 29.

47. Use of a virus, preferably an adenovirus, according to any of claims 1 to 29, whereby the virus comprises a nucleic acid coding for a transgene.
48. Use of a virus, preferably an adenovirus, according to any of claims 1 to 29, whereby the virus comprises the translation and/or transcription product of a transgene.
49. Use of an adenoviral replication system according to claim 36 or 37, whereby the nucleic acid of the adenoviral replication system and/or the nucleic acid of the helper virus comprises a transgene or a nucleic acid coding for a transgene.
50. Use of a nucleic acid according to any of claims 38 to 42, whereby the nucleic acid comprises a transgene or a nucleic acid coding for a transgene.
51. Use according to any of claims 47 to 50, whereby the transgene is selected from the group comprising prodrug genes, cytokines, apoptose-inducing genes, tumor suppressor genes, genes for metalloproteinase inhibitors and genes for angiogenesis inhibitors.
52. Use according to any of claims 47 to 50, whereby the transgene is selected from the group comprising nucleic acids for siRNA, for aptamers, for antisense molecules and for ribozymes, whereby the siRNA, the aptamer, the antisense molecule and/or the ribozyme are targeting a target molecule.
53. Use according to claim 52, whereby the target molecule is selected from the group comprising resistance relevant factors, anti-apoptosis factors, oncogenes, angiogenesis factors, DNA synthesis enzymes, DNA repair enzymes, growth factors, receptors for growth factors, transcription factors, metalloproteinases, preferably matrix metalloprotein kinases, and plasminogen activator of the urokinase type.
54. Use according to any of the preceding claims, whereby the medicament further comprises a pharmaceutically active compound.
55. Use according to claim 54, whereby the pharmaceutically active compound is selected from the group comprising cytokines, metalloproteinase inhibitors, angiogenesis inhibitors,

cytostatics, cell cycle inhibitors, proteasome inhibitors, recombinant antibodies, inhibitors to the signal transduction cascade and protein kinase.

56. Use according to any of the proceeding claims, characterized in that the medicament comprises a combination of at least two agents, whereby each and any of the agent is individually and independently selected from the group comprising cytostatics.

57. Use according to claim 56, characterized in that at least two of the agents address different target molecules.

58. Use according to claim 57, characterized in that at least two of the agents act through a different mode of action.

59. Use according to any of claims 56 to 58, characterized in that at least one agent increases the capacity of a cell to be infected in which the virus replicates.

60. Use according to any of claims 56 to 59, characterized in that at least one agent influences the availability of a component of the cell, preferably increases the availability of their component, whereby the component mediates the uptake of the virus.

61. Use according to any of claims 56 to 60, characterized in that at least one agent mediates the transport of YB-1 into the nucleus, preferably increases said transport.

62. Use according to any of claims 56 to 61, characterized in that at least one agent is a histone deacylase inhibitor.

63. Use according to claim 62, characterized in that the histone deacylase inhibitor is selected from the group comprising Trichostatin A, FR 901228, MS-27-275, NVP-LAQ824, PXD101 Apicidin and Scriptaid.

64. Use according to any of claims 56 to 62, characterized in that at least one agent is selected from the group comprising Trichostatin A, FR 901228, MS-27-275, NVP-LAQ824, PXD101 Apicidin and Scriptaid.

65. Use according to any of claims 56 to 64, characterized in that at least one agent is a topoisomerase inhibitor.
66. Use according to claims 65, characterized in that the topoisomerase inhibitor is selected from the group comprising Camptothecin, Irinotecan, Topotecan, DX-895If, SN-38, 9-aminocamptothecin, 9-nitrocamptothecin, Daunorubicin and Etoposid.
67. Use according to any of the preceding claims, characterized in that the agent comprises Trichostatin A and Irinotecan.
68. Use according to any of the preceding claims, characterized in that the virus, in particular the virus according to any of the preceding claims, is separated from the at least two agents.
69. Use according to claim 68, characterized in that at least one unit dose of the virus is separated from at least one unit dose of one or the at least two agents.
70. Kit comprising a virus, preferably a virus according to any of the preceding claims, and at least two agents, whereby any agent is individually and independently selected from the group comprising cytostatics.